

ORGANIC ACID DISORDERS

3- Methylcrotonyl-Coenzyme A Carboxylase (3-MCC) Deficiency

This disorder is caused by a shortage of an enzyme that is needed to breakdown proteins containing amino acid leucine. Infants with 3-MCC deficiency appear normal at birth but usually develop symptoms in infancy or early childhood. Characteristic features of the condition range from mild to life threatening, included feeding difficulties, recurrent episodes of vomiting, diarrhea, and muscle weakness.

Screening Method:

Tandem Mass Spectrometry method to identify increased level of C5 hydroxy acylcarnitine (C5-OH).

Treatment:

Reduced protein intake, particularly the amino acid leucine. Carnitine supplementation may be indicated. Avoid prolonged fasting and travel with letter of treatment guidelines.

Incidence:

1: 75,000 births

Methylmalonic Acidemias (MMA)

MMA can result from several different genetic disorders, including Methylmalonic-CoA mutase deficiency and defects of enzymes in vitamin B12 metabolism. The symptoms of this disorder are vomiting, dehydration, respiratory distress, and muscle weakness, that can lead to coma or death. A long term complication is renal failure.

Screening Method:

Tandem Mass Spectrometry method used to measure levels of three-carbon acylcarnitine (C3).

Treatment:

Reduced protein intake, particularly amino acids, Valine, Isoleucine, Methionine, and Threonine. There are commercially available formulas meeting this dietary requirement. Oral antibiotics to help control infections.

Incidence:

1: 50,000 births

Beta-Ketothiolase (BKT) Deficiency

BKT deficiency is an inherited disorder in which the body can not breakdown the amino acid, Isoleucine. The deficiency of this enzyme impairs the body's ability to process ketones, which are molecules produced during the breakdown of fats. Signs and symptoms usually appear between the ages of 6 - 24 months. Affected children present with episodes of vomiting, dehydration, respiratory distress, extreme tiredness, and occasionally seizures. Ketoacidotic attacks are triggered by infections, fasting or intake of protein-rich foods, and can lead to coma.

Screening Method:

Elevated level of C5:1 (tiglylor 3-methylcrotonyl carnitine) measured by Tandem Mass Spectrometry method.

Treatment:

Aggressively treat acute acidosis. Avoid fasting, eat frequently and restrict protein intake. Intravenous glucose can be used when child is vomiting or has a fever. Monitor urinary ketones for metabolic crisis.

Incidence:

Very rare- < 50 cases reported since 1971

Isovaleric Acidemia (IVA)

IVA results from a defect in metabolism of the amino acid, Leucine. There are 2 types of this disorder. The acute neonatal form presents within the first weeks of life with poor feeding, vomiting, severe ketoacidosis progressing to coma and death. Most will have a characteristic odor of "sweaty socks" from elevated blood levels of isovaleryl acids. The chronic intermittent form presents later in infancy or childhood with episodes of metabolic acidosis usually associated with illness or increased protein intake.

Screening Method:

Use of Tandem Mass Spectrometry to measure elevated level of C5 (isovaleryl/2 methylbutyryl carnitine).

Treatment:

Avoidance of fasting, low protein diet with restricted Leucine, in combination with glycine and Carnitine supplements.

Incidence:

1:50,000

Glutaric Acidemia Type 1 (GAI)

GAI is caused by the deficiency of the enzyme that helps break down the amino acids Lysine, Hydroxy lysine, and Tryptophan. The severity of this disorder varies, in most cases symptoms first occur in infancy or early childhood. Some babies born with GAI have unusually large heads. Affected children have difficulty moving and may experience spasms, jerking, rigidity, or decreased muscle tone. Some experience bleeding in the brain or eyes that could be mistaken for child abuse.

Screening Method:

Test for the presence of glutaric acid covalentbound to Carnitine (C5-DC) using Tandem Mass Spectrometry.

Treatment:

Aggressive treatment of clinical symptoms with fever control, IV fluids, including glucose and carnitine with monitored administration of insulin. Parents should travel with a letter of treatment guidelines.

Incidence:

1:30,000 births

3-Hydroxy-3-Methylglutaryl -CoA Lyase (HMG) Deficiency

This enzyme plays an important role in breaking down dietary proteins and fats for energy. It has a dual function in processing the amino acid leucine and regulating production of Ketone bodies. The signs and symptoms of this disorder usually appear within the first year of life. The symptoms are episodes of vomiting, diarrhea, lethargy, weak muscle tone, and low blood sugar. If untreated, it can lead to breathing problems, convulsions, coma, and death.

Screening Method:

Tandem Mass Spectrometry method is used to detect elevated levels of C5-hydroxy acylcarnitine (C5-OH) and 6 carbon dicarboxylic acylcarnitine (C6-DC).

Treatment:

Acute symptoms should be treated with IV glucose, bicarbonate, and protein(leucine) restriction. Long term treatment; avoid fasting and restrict protein intake.

Incidence:

1: 300,000 births.

Multiple Carboxylase Deficiency (MCD)

The two defects in biotin metabolism associated with MCD are caused by deficient activity of holocarboxylase synthetase and biotinidase. The infants affected with deficient holocarboxylase synthetase present in the first weeks of life with poor feeding, lethargy, muscle weakness, and seizures that can progress to coma. They also have metabolic acidosis and can exhibit a generalized rash. In contrast, Biotinidase deficiency, which constitutes the vast majority of patients with MCD, typically present after several months of life with developmental delay, muscle weakness, seizures, hearing loss and skin rash. The disease can be life threatening.

Screening Method:

Tandem Mass Spectrometry Method is used to detect elevated levels of C5-hydroxy acylcarnitine (C5-OH).

Treatment:

Both enzyme defects respond to administration of high doses of biotin.

Incidence:

1: 50,000

Propionic Acidemia (PA)

Propionic Acidemia is caused by the accumulation of propionic acid due to the deficiency in Propionyl CoA Carboxylase, a biotin dependent enzyme needed to break down amino acids. Infants usually present in the first days of life with refusing to feed, vomiting, muscle weakness, and elevated level of blood ammonia. Seizures, low white cell and platelet counts and enlarged liver may be present. If left untreated they can progress to coma and die. Some patients present later in infancy with acute encephalopathy, ketoacidosis and developmental delay.

Screening Method:

Tandem Mass Spectrometry method used to detect elevated levels of three-carbon acylcarnitine (C3).

Treatment:

A special metabolic formula restricted in the amino acids, valine, isoleucine, methionine, and threonine; Carnitine supplementation and oral antibiotics to control infections.

Incidence:

1: 50,000

